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Halve-dose Magnesium Sulphate Regimen Compared to the Pritchard Regimen in the Management of Pre-eclampsia and Eclampsia: A Prospective Single Blind Randomized Study in a Private Hospital

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Abstract

Hypertensive diseases in pregnancy constitute a major concern and it is a major cause of maternal and perinatal morbidity and mortality worldwide and especially in the resource-challenged countries. Regimens for administration of magnesium sulphate have evolved over the years with different regimens being advocated. Objective: to compare the effectiveness of halve-dose regimen of magnesium sulphate therapy with standard Pritchard regimen in the management of patients with either pre-eclampsia or eclampsia. Result: out of 1,699 deliveries recorded during the period of study 74 patients that met the inclusion criteria were recruited for this study 75.7% presented primarily with pre-eclampsia while 24.3% presented with eclampsia primarily. Booked patients were 52.7% while 47.3% were unbooked. There were two arms of this study; the standard Pritchard and the half-dose regimen arms. The standard Pritchard regimen arm had 36 subjects while the half-dose regimen had 38 subjects respectively. The same number of subjects in the two arms progressed from pre-eclampsia to eclampsia. There were more patients with recurrent convulsion in the standard Pritchard regimen arm compared to the half-dose regimen though this was not statistically significant.

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Case fatality was 1.35% and it was due to HELLP syndrome. Neonatal admission and mortality were not significantly different between the two arms of the study. Patients' satisfaction was generally more in the half-dose regimen arm. Conclusion: from this study it is shown that giving half the dose of the standard Pritchard regimen is as effective as the standard Pritchard regimen itself. The import of this is that the risk of complications arising from magnesium sulphate is reduced, cost of treatment is also less, and overall general patient satisfaction is encouraging.

Keywords: half-dose regimen; Pritchard regimen; eclampsia; pre-eclampsia; magnesium sulphate.

1. Background

Hypertensive diseases in pregnancy constitute major concern amongst Obstetricians. It is a major cause of maternal and perinatal morbidity and mortality worldwide, especially in low resource countries [1]. Hypertension is common during pregnancy and around 10% of women will have their blood pressure recorded as above normal at some point during the antenatal period before delivery [2]. It is estimated to complicate about 5% of all pregnancies and 11% of first pregnancies [3]. Pre-eclampsia is defined as hypertension and significant proteinuria beginning during the second half of gestation in a previously normotensive and non-proteinuric pregnant woman [3,4]. It complicates 4-8% of all pregnancies [5,6]. Eclampsia on the other hand, is the new onset of grand mal seizures occurring during or after pregnancy that do not have another identifiable cause [7,8]. It could also be defined as the development of convulsions and/or unexplained coma during pregnancy or postpartum in patients with signs and symptoms of pre-eclampsia [9]. Incidence of eclampsia in developed countries ranges from 5 to 7 cases per 10,000 deliveries [10], quite unlike in developing countries where Nigeria belongs, where the prevalence ranges from 2 to 16.7% [11-13]. Pre-eclampsia and eclampsia are not distinct disorders but the manifestation of the spectrum of clinical symptoms of the same condition [10]. Once eclampsia occurs the risk to mother and foetus[es] is substantial. The World Health Organization (WHO) estimates that the incidence of pre-eclampsia is seven times higher in the low and middle –income countries than in high-income countries, and the risk of a woman in a low-income country dying from either pre-eclampsia or eclampsia is three hundred times that of a woman in a high-income country [7,14].

Globally, pre-eclampsia and eclampsia account for 10-15% of maternal deaths [15]. Unlike in the developed countries where pre-eclampsia and eclampsia are associated with near-miss rather than maternal death, death usually results from eclampsia in the developing countries [16].

To date, the aetiology of pre-eclampsia has remained poorly understood but it has been documented that pre-eclampsia is polygenetic and is caused by a combination of maternal and foetal genes with influence of environmental factors [17]. Pathogenesis of eclamptic convulsions has also remained source of controversy [9]. Magnesium sulphate was one of the earliest drugs suggested to have specific anticonvulsant action in the treatment of eclampsia[18]. Regimens for administration of magnesium sulphate have evolved over the years, but have not yet been formally evaluated [18]. Different regimens have been advocated by different experts in different countries [1,2,19,20]. Incidentally advocates for lower doses and shorter duration of treatment regimen have been more in the low resource countries where the cost of purchase of magnesium sulphate constitute a

large chunk of the total cost of treating pre-eclampsia and/or eclampsia [18,19]. The great concern for magnesium sulphate therapy is the risk of the toxicity which could increase with duration of treatment and dose especially if monitoring of patient is suboptimal [19]. Average cost of an ampoule of 50% magnesium sulphate in a private hospital in Nigeria may be beyond the reach of most people and with standard Pritchard regimen where a patient will require minimum of 45g of magnesium sulphate before discharge, the cost is better imagined for an already impoverished populace, likewise the intramuscular route can cause so much pain even though the ease of administration cannot be over-looked, therefore less dose of intramuscular injection is tantamount to less pain and patient's satisfaction.

The exact mechanism of action of magnesium sulphate is unclear [2,19]. It may cause vasodilatation and subsequent reduction of cerebral ischaemia [21]. Alternatively it may have partial or total effect on N-methyl-D-aspartate (NMDA) in the brain [2]. These NMDA receptors are activated in response to asphyxia, leading to calcium influx into the neurons, which causes cell injury [2]. It is suggested that magnesium may block these receptors, so reducing calcium influx thereby protecting the neurons from damage [2]. The objective of this study was to compare the effectiveness of halve-dose regimen of magnesium sulphate therapy with the standard-dose Pritchard regimen in the management of patients with either pre-eclampsia or eclampsia

1.1 Methodology

This study was a prospective single-blind randomized study that spanned over a 12month period starting from January 1st 2017 to December 31st 2017 in the Obstetrics and Gynaecology unit of Sacred Heart Hospital, Lantoro, Abeokuta in Ogun State. The hospital is a 300 bedded hospital with the Obstetrics and Gynaecology unit having 88beds in various parts of the department. The hospital is the first hospital in Nigeria with clienteles from the whole of the South-West of Nigeria as well as the Republic of Benin. All consenting pregnant women that had pre-eclampsia or eclampsia from 28weeks in our environment who presented to the antenatal clinic during the antenatal period, in labour or postpartum and who met the inclusion criteria were recruited into the study. However, patients with multiple gestation, renal disease or diabetes mellitus, those who already had magnesium sulphate therapy before presentation, and those that declined to participate were excluded from the study. At presentation each patient or her relative picked a sealed unlabeled envelope that contained either standard dose regimen or half dose regimen slip. This enabled the attending midwife or doctor to know the regimen to use for the patient. This was done after consent was obtained. A written informed consent was obtained from both the patients that were conscious and the relatives of those that were not conscious enough following which a designed pro-forma was used to obtain necessary information that was relevant to the study. For the purpose of this study significant hypertension and proteinuria were as defined by the International Society for the Study of Hypertension in Pregnancy (ISSHP), which are blood pressure of ≥140/90mmHg and proteinuria of ≥2+respectively. Korotkoff phase V was used to designate the diastolic blood pressure. At presentation at the clinics, antenatal ward, labour ward, or the postnatal ward the blood pressure of each subject was taken in the supine position with a left lateral tilt using an Accoson table-top mercury sphygmomanometer that had the appropriate size cuff with the arm at the level of the heart. The mid-stream urine sample obtained was tested with combi-9 urinalysis strip for proteinuria to make a diagnosis of pre-eclampsia or eclampsia. Height was measured with each subject standing barefooted on a standard Seca Stadiometer. The height was

read from under the head piece on the calibrated meter of the stadiometer to the nearest 0.1cm. Weight was measured using a calibrated weighing scale (Camry digital weighing scale) without shoes and subjects wearing light clothes; weight was read to the nearest 0.1kg. All these were done at presentation for those who were conscious while the measurements of those that presented in a state of unconsciousness were done after they had regained consciousness. Before discharge the satisfaction of each patient was assessed using "Short Assessment of Patient's Satisfaction" tool was used. Analysis of data was done with Statistical Package for Social Science Students (SPSS) version 21.

1.2 Primary outcomes

- Eclampsia for those with pre-eclampsia, or recurrent convulsion for those with eclampsia
- Death of baby before discharge from the hospital

1.3 Secondary outcomes

- Maternal death
- Admission and length of stay in the hospital
- Admission and length of stay in the special care baby unit (SCBU)

2. Results

During the course of this study which was between January 1st 2017 and December 31st 2017 the unit recorded 1,699 deliveries out of which 74 patients were either managed for pre-eclampsia or eclampsia using the standard Pritchard regimen or half-dose regimen. As depicted in **table 1**, 39(52.7%) of the patients were booked while 35(47.3%) were unbooked. Ages of 25 to 29years accounted for 31.1% while those that were 40years and above accounted for 6.8%. 29.7% were primipara, 25.7% were primigravidae, and 5.4% were grandmultipara. 45.9% were between the gestational age of 38 and 42weeks; and only 18.9% presented at the gestational age of 28 to 32weeks. **Figure 1** shows the diagnosis at presentation; out of the 74 patients that were recruited for this study 56(75.7%) had pre-eclampsia at presentation while 18(24.3%) had eclampsia at presentation. **Figure 2** shows patient distributions in the two arms of the study; in the Pritchard regimen 10 patients had eclampsia at presentation while the remaining 26 patients had pre-eclampsia; in the half-dose regimen arm 8 patients had eclampsia primarily while the remaining 30 had pre-eclampsia at presentation. **Table 2** shows the number of patients with pre-eclampsia in the Pritchard regimen arm and the Half-dose regimen arm that progressed to eclampsia to be equal; this finding was shown not to be statistically significant. The **table 3** displays the number of patients in the two arms of the study that had recurrent convulsion despite therapy, there was no statistical significance between the two groups. The only maternal mortality recorded was in the Pritchard regimen arm as shown in **table 4** making the case fatality rate to be 1.35%. **Table 5** shows that 15 neonates were admitted into the neonatal intensive care unit in the Pritchard regimen arm while in the half-dose regimen arm 18 neonates were admitted into the neonatal intensive care unit with no statistically significant relationship. **Figure 3** shows the number of neonatal deaths in the Pritchard regimen as well as those that occurred in the half-dose regimen arm with no statistically significant relationship. The duration of admission as depicted in **table 6** showed that in

the Pritchard regimen arm 12 patients spent 4days or less on admission while 24 patients spent more than 4days while in the half-dose regimen arm 15 patients spent 4days or less on admission and 23 patients spent more than 4days on admission with statistically significant relationship and there was no statistically significant relationship. **Table 7** revealed that 25 patients expressed excellent satisfaction with the half-dose regimen compared to only 7patients in the Pritchard regimen arm; only a patient was indifferent to the half-dose regimen compared to none in the Pritchard regimen arm.

Table 1: Sociodemographic characteristics of subjects

	N=74	Percentage (%)
Booking status		
Booked	39	52.7
Unbooked	35	47.3
Age range		
15-19	2	2.7
20-24	12	16.2
25-29	23	31.1
30-34	21	28.4
35-39	11	14.9
≥40	5	6.8
Parity		
0	19	25.7
1	22	29.7
2	17	23.0
3	8	10.8
4	4	5.4
≥5	4	5.4
Gestational age		
28-32	14	18.9
33-37	26	35.1
38-42	34	45.9

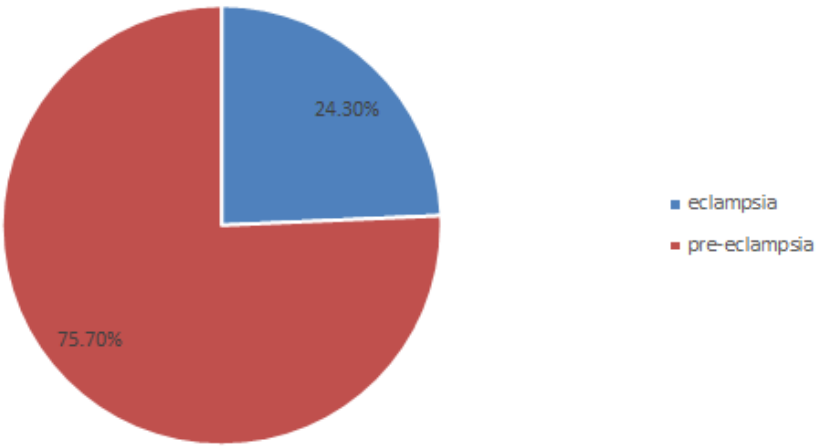

Figure 1: Diagnosis at presentatiuon

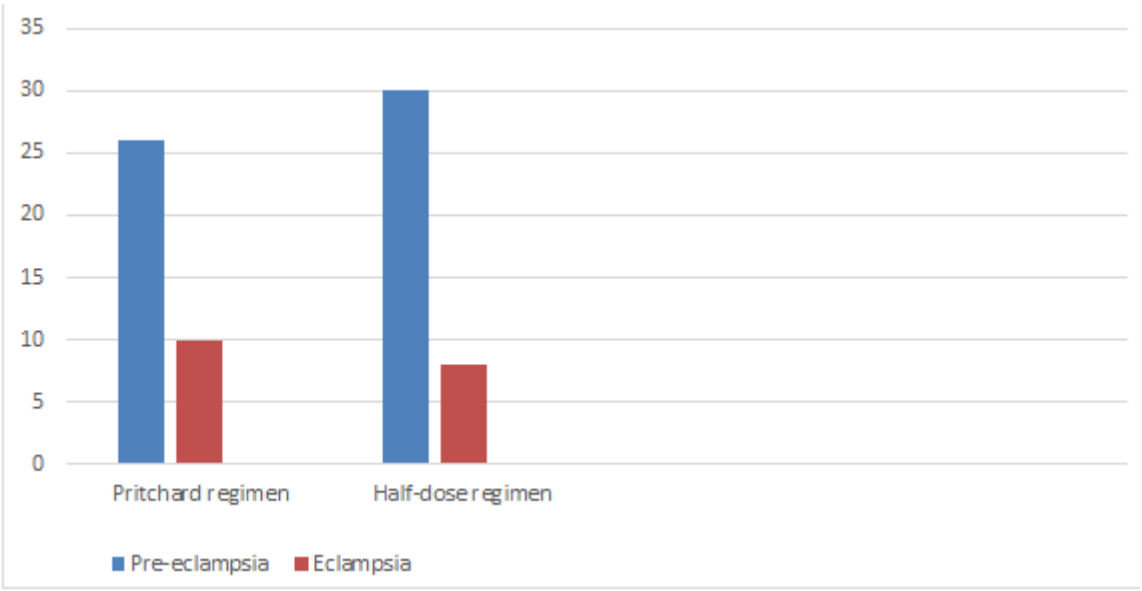

Figure 2: Chart showing the number of subjects in the tow arms of the investigation

Table 2: Number of patients with pre-eclampsia that developed eclampsia while on either Pritchard or half dose regimen

		Yes	None	X^2
Regimen	**Pritchard**	7	29	0.013
	Half dose	7	31	
	Total	**14**	**60**	

Table 3: Number of patients with eclampsia on either Pritchard or half dose regimen that had recurrent convulsions

		Yes	None	X^2
Regimen	**Pritchard**	10	26	2.445
	Half dose	5	33	
	Total	**15**	**59**	

Table 4: Maternal mortality compared against the regimen used

		Yes	None
Regimen	**Pritchard**	1	35
	Half dose	0	38
	Total	**1**	**73**

Table 5: Regimen compared to NICU neonatal admission

		Yes	None	X^2
Regimen	Pritchard	15	21	
	Half dose	18	20	
	Total	**33**	41	**0.243**

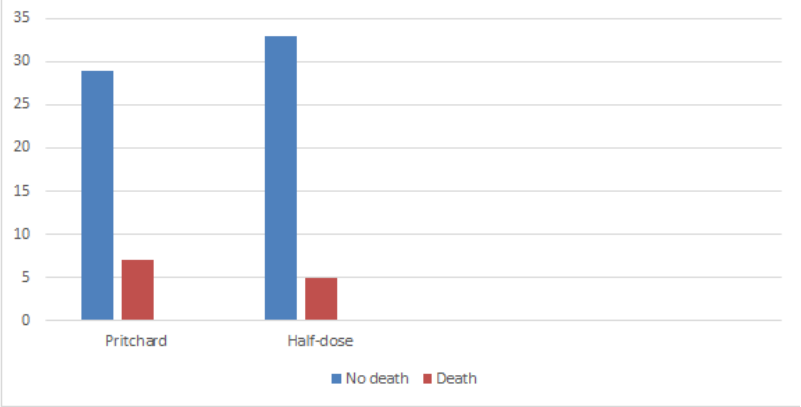

Figure 3: Neonatal mortality compared against the regimen used in the two arms of the study

X^2 = 0.538

Table 6: Regimen compared to duration

		Duration of hospital stay			
		≤4 days	**>4days**	**Total**	**X2**
Regimen	**Pritchard**	12	24	36	
	Half dose	15	23	38	
	Total	**27**	**47**	**74**	**0.301**

Table 7: Regimen against patients' satisfaction

		Excellent	Very good	Good	Not good	Indifferent
Regimen	**Pritchard**	7	13	13	3	0
	Half-dose	25	10	2	3	0
	Total	**32**	**23**	**15**	**6**	**0**

3. Discussion

During the period of study the department recorded 1,699 deliveries out of which 18 of them had eclampsia while 56 patients had pre-eclampsia, this makes the incidence of eclampsia and pre-eclampsia to be 1.06% and 3.3% respectively. The incidence of eclampsia is low compared to findings in most studies carried out in public institutions in Nigeria, however the incidence of pre-eclampsia is comparable to the findings in some public health institutions in the country [17, 19, 20, 22], the reason for these disparities could be because of the likelihood of presentation in other private or public health facilities.

Interestingly it is said that PET/eclampsia is often associated with primigravidity the findings of this study say otherwise for the patients with one and two previous deliveries were more than the primigravidae, the reason for this is not clear-cut; this finding might have been influenced by environmental or dietary factors [17] though these were not part of this present study.

It is without prejudice that magnesium sulphate is very effective in preventing eclampsia in patients with pre-eclampsia and recurrent convulsions in the eclamptics. In the two arms of this study the number of patients that progressed to eclampsia from pre-eclampsia is the same; this goes to show that development of convulsion may be independent of the dose of magnesium sulphate administered to a patient, also compared to the Pritchard regimen arm there were less number of patients that developed recurrent convulsion in the half-dose regimen though the finding was not statistically significant. The import of these findings are: (i) less dose of the magnesium sulphate may be needed to either treat pre-eclampsia or prevent eclampsia thereby reduction in the cost of treatment, (ii) the risk of complications that may arise from magnesium sulphate therapy will be remarkably reduced.

There was only one maternal mortality recorded making the case fatality rate to be 1.35% this is rather lower than the findings by other authors in public institutions [7,12,19,20]. This death occurred in the Pritchard regimen arm however this does not imply magnesium sulphate caused the death because the patient died as a result of HELLP syndrome. Ironically there were more neonatal death in the Pritchard arm of the study, it is difficult to adduce that the dose of the magnesium sulphate could have accounted for this without taking into consideration the primary disease itself which can lead to either maternal or neonatal morbidity/mortality.

Compared to Pritchard regimen patients were generally more satisfied in the half-dose regimen arm using the Short Assessment of Patient Satisfaction (SAPS) developed by the center for Health Service Development of University of Wollongong [24].

4. Conclusion

The study revealed that giving half the dose of the standard Pritchard regimen is as effective as the standard Pritchard regimen itself. The import of this is that the risk of complications arising from magnesium sulphate therapy is reduced, cost of treatment is also less, and overall general patient satisfaction is encouraging.

5. Constraints/limitations

The sample size was too small to draw a conclusion that half-dose magnesium sulphate regimen is as effective as the standard dose regimen however, with proper patient selection a lot of benefits could be derived from half-dose regimen. It was difficult to determine the accuracy of the gestational age in the unbooked patients since they did not have the benefit of having an early ultrasound scan.

6. Recommendation

Giving halve the dose of the standard Pritchard regimen that is normally required traditionally is as effective as the standard regimen with less cost and better patient's satisfaction. It will also prevent some of the complications associated with magnesium sulphate since the safety margin of the drug is small. A larger multicenter study may be required before an outright recommendation for the use of half dose regimen.

References

[1]. S Dasgupta, A Sarkel, A Jain. "Single Loading Dose of magnesium Sulphate in Severe Pre-eclampsia and Eclampsia – Is it Effective? A prospective Study". Obstet Gynecol Int. J. 2(6):00659,2015

[2]. L Duley, DJ Henderson-Smart, G.J.A Walker. "Interventions for preventing pre-eclampsia and its consequences: generic protocol (Protocol)." The Cochrane Library. 2:1-14.2009

[3]. GJ Hofmeyr, L Duley, A Atallah. "Dietary calcium supplementation for prevention of pre-eclampsia and related problems: a systemic review and commentary." Br. J. Obstet Gynaecol 114:933-943,2007

[4]. FG Cunningham, KJ Leveno, S.L Bloom, J.C Hauth, D.J Rouse, C.Y Spong (Eds). "Pregnancy Hypertension", in Williams Obstetrics 23rd Edition, McGraw-Hills companies 2010; pp. 706-756.

[5]. DI Miller. "Hypertension in pregnancy", in: Current Diagnosis and Treatment Obstetrics and Gynaecology, 10th edition, AH Decherney, L Nathan, TM Goodwin and N Laufer (Eds), McGraw-Hill Medical Publishing Division 2007; pp 321- 327.

[6]. K Sukonpan, V Phupong. "Serum calcium and serum magnesium in normal and pre-eclamptic pregnancy." Arch Gynaecol Obstet 2005; 273:12-16.

[7]. Engender Health. "BALANCING THE SCALES". Expanding treatment for pregnant women with life-threatening hypertensive conditions in developing countries. A report on Barriers and solutions to Treat Pre-eclampsia and Eclampsia. New York: Engender Health; 2007

[8]. MB Sibai, MA Villar, E Bray. "Magnesium supplementation during pregnancy: a double-blind study." Br. J. Obstet Gynaecol. 1988; 950:120-5.

[9]. BM Sibai. "Diagnosis, Prevention, and Management of Eclampsia," Obstet Gynecol 2005; 105:402-10

[10]. KO Osungbade, OK Ige. "Public Health Perspectives of Pre-eclampsia in Developing Countries: Implication for Health system strengthening." Journal of Pregnancy [Review]. 2011; 2011:1-6

[11]. Population Council Nigeria. "Administering Magnesium Sulphate to Treat severe Pre-eclampsia and Eclampsia," 2009.Available at http://.popcouncil.org/script/tellafriend.asp.

[12]. FE Olopade, TO Lawoyin. "Maternal Mortality in a Nigerian Hospital." Afr J Biomed Research, 2008;11(3):276-273

[13]. A Omole-Ohonsi, AO Ashimi. "Pre-eclampsia: a study of risk factors." Nigerian Medical Practitioner 2008; 53(6):99-102

[14]. A Gaym, P Barley, L Pearson, K Admasu, Y Gebrehiwot. "Disease burden due to Pre-eclampsia/eclampsia and Ethiopian health system's response." Int J Gynecol Obstet; 2011;115:112-116

[15]. JATurner. "Diagnosis and management of pre-eclampsia: an update." Int J Women's Health, 2010;2:327-337

[16]. L Duley. "The global impact of Pre-eclampsia and Eclampsia." Semin Perinatol, 2009;33:130-137

[17]. ET Agida, BI Adeka, KA Jibril. "Pregnancy outcome in Eclamptics at the University of Abuja Teaching Hospital, Gwagwalada, Abuja: A 3year review." Nigerian J of Clinical Practice 2010;13(4):394-398

[18]. L Duley, HE Matar, MQ Almerie, D.R Hall. "Alternative Magnesium Sulphate regimens for women with pre-eclampsia and eclampsia (Review)." © 2010(8) The Cochrane Collaboration

[19]. AE Bisallah, M Danjuma, NB Lawal, MN Ibrahim. "Magnesium therapy in eclampsia: Sokoto (Ultra short) regimen." BMC Research Notes 2009,2;165 doi:10.1186/1756 – 0500-2-165

[20]. N Jana, S Dasgupta, AK Das, D Santra, B Samanta. "Experience of a low-dose magnesium sulfate regimen for the management of eclampsia over a decade." Int.J Gynecol Obstet (2013), http://dx.doi.org/10.1016/j.ijgo.2013.01.029

[21]. MA Belfort, KJ Moise. "Effect of Magnesium sulphate on maternal brain blood flow in Pre-eclampsia: a randomized, placebo controlled study." Am J Obstet Gynecol 1992;167;661-6

[22]. O Abiodun, OA Oguntayo, AI Sambo. "Serum levels of calcium and magnesium in pre-eclamptic-eclamptic patients in a tertiary institution." It. J. Gynaecol. Obstet. 2015, 27: 101-110 N.3 DOI: 10.14660/2385-0868-23

[23]. O Olusanya, EE Okpere, M Ezimokhai. "The importance of socioeconomic class in voluntary fertility in a developing country." W Afr J Med 1985;4:205-12

[24]. Center for Health Service Development. "The Short Assessment of Patient Satisfaction (SAPS)." University of Wollongong pp1-2